REMARKS

The instant amendment presents new claims 23-30, which respectively add to each of claims 15-22 the further element that the composition or method is one that conceives of twice-daily administration, or what is commonly known in the art as BID dosing.

While the Advisory Action informs that Applicants' previous arguments in response to the final rejection have been fully considered and were found to be unpersuasive, the Examiner's reluctance to *discuss* and *distinguish* those arguments in her Advisory Action comments would tend to suggest that they were in fact not considered at all, or if considered, were found to be insurmountable and were for that reason not commented upon.

The Examiner asserts in the latest comments that Sims "specifically" teaches "ibuprofen, carbetapentane, and guaifenesin" yet offers no citation to column or line because, as argued by Applicants at length in previous responses, Sims does *not* "specifically" teach any combination of carbetapentane and guaifenesin, much less does it specifically teach the claimed carbetapentane *tannate* salt. Sims *does* disclose the use of the (*S*)-enantiomer of ibuprofen in combination with component elements selected from various and separate Markush groups.

These several separate Markush groups are directed to myriad antitussives (col. 1., lines 38-43), myriad expectorants (col. 1., lines 44-47), an *unlimited* number of salts of those free bases of the antitiussives or expectorants (col. 2, lines 37-39), nine different delivery forms (col.3, lines 39-41) and infinite dosage ranges having absolutely no

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specificity in relation to any of the myriad active ingredients (col. 3, lines 31-38). In their earlier arguments Applicants stressed that a piecemeal selection from amongst these disclosed groupings would result in a minimum of 1760 permutations to toil through before the artisan would derive the exact combination of active ingredients, salts, delivery form, and dosage amounts instantly claimed. Rather than debate that fact the Examiner glosses over it and characterizes this staggering number of variations as "not unreasonable" and "envisaged."

As earlier argued, the Graham v. John Deere test for obviousness has nothing to do with the number of combinations disclosed by the prior art as being "not unreasonable" or "envisaged," it requires that the Examiner (1) determine the scope and content of the prior art, (2) ascertain its differences from the claimed invention, (3) resolve the level of ordinary skill in the art, and (4) evaluate evidence of secondary considerations of factors suggesting non-obviousness. 383 U.S. 1, 17 (1966). The resolute dismissiveness of the comments in the Advisory Action betrays that no such analysis has been undertaken!

Ignoring the U.S Supreme Court's mandate in Graham v. John Deere, the Examiner chooses instead to hang her hat on MPEP 2144.04 for the proposition that "the omission of an element and its function is obvious if the function of the element is not **desired**." The last word of that statement is the undoing of the Examiner's position. As was repeatedly argued in earlier responses, the mere fact that the prior art *can* be modified in the manner argued by the Examiner does not make the modification obvious "**unless the prior art suggested the desirability of the modification.**" In re Gordon, 733 F.2d 900, 902 (Fed. Cir. 1984). Applicants' here repeat the string citation of Federal

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Circuit precedents wherein that court has consistently *reversed* obviousness determinations by the Board based upon Gordon's principle, the while quoting the above cited Gordon language. In re Laskowski, 871 F.2d 115, at 117 (1989). In re Mills, 916 F.2d 680, at 682 (1990). In re Fritch, 972 F.2d 1260, at 1266 (1992). In re Debus, 1993 WL 513890, at **1 (1993). In re Brouwer, 77 F.3d 422, at 425 (1996). In re Butler, 1999 WL 164952, at **2 (1999). It is clearly the position of the Federal Circuit, and should unquestionably be the position of the Office, that the learned Examiner must isolate that teaching in the whole of the prior art that commends to the artisan the **desirability** of the modification she proposes to meet the subject claims.

In the instant case the Examiner's proposed modification is *not* obvious because she has failed to indicate where, within Sims' teaching, Sims suggests that it would be **desirable** to abandon its ibuprofen (analgesic / anti-inflammatory) component. This is because Sims offers no such suggestion. As earlier argued, the only component that Sims would suggest the abandonment of is the expectorant, which Sims refers to as being *optional*. Such a suggestion teaches away from the instant claims since guaifenesin is an essential element of the present invention. And Sims could not teach or suggest *any* modification that conceives of abandoning its ibuprofen component because Sims' unwavering focus is the treatment of ***pain*** and ***inflammation*** regardless of its cause:

> "This invention relates to pharmaceutical compositions for use in **the treatment of pain and inflammation** and the relief of cough cold symptoms..." (col. 1, lines 31-33, emphasis added).
>
> "This invention is also directed to a method of **treating pain and inflammation** and the relief of cough and cold symptoms..." (col. 1, lines 48-50, emphasis added).
>
> "This invention is also directed to a method of eliciting an onset hastened and enhanced response for **the treatment of pain and inflammation** and

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> the relief of cough and cold symptoms..." (col 1, lines 65-68, emphasis added).

The Examiner argues that "Sims et al. teaches a composition for the treatment of pain and inflammation **due** to cough and cold wherein the antitussive agent acts as a cough suppressant and the expectorants relieves congestion." But both the above excerpts and Sims as a whole would not support such a reading. It is clear that the prime focus of Sims is to treat pain and inflammation without any mention of its being "**due**" to cough and cold. From the Examiner's contrary assertion she concludes that the omission of the analgesic (ibuprofen) "would still render a composition that relieves cough and cold symptoms due to the antitussive and expectorant agents[.]" While Applicant's do not oppose that conclusion, they stress that Sims does not teach or even remotely suggest the modification that the Examiner proposes:

> "The composition and methods of the present invention may be used to **treat pain and inflammation, or pain alone or inflammation alone where only one is present**, along with the treatment of cough and cold symptoms." (column 2, lines 16-19, emphasis added).

The above except clearly demonstrates that notwithstanding the Examiner's arguments, one of ordinary skill in the art would **not** reformulate Sims on the basis of undesired elements or functions. That Sims considers the *inclusion* of an analgesic to be of critical importance is clear from its laudatory rhetoric regarding the *improved pain relief* advantages that ibuprofen's *S*-enantiomer brings to antitussive combinations, over racemic ibuprofen formulations:

> "The utilization of (S)-ibuprofen in an analgesic/antitussive combination offers significant advantages over the combination of racemic ibuprofen with an antitussive. (S)-ibuprofen provides a **faster onset of pain relief and an enhanced degree of relief compared to racemic ibuprofen. These benefits are increased in an (S)-ibuprofen/antitussive combination as the antitussive may potentiate the action of the (S)-**

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> **ibuprofen.** This has not heretofore been observed because the art has not proposed the combination of the (S)-ibuprofen enantiomer, absent (R)-ibuprofen, with an antitussive. **Furthermore the antitussive also may potentiate the duration of the analgesic and anti-inflammatory response.** The presence of the (R)-ibuprofen may blur the potentiated effect." (column 2, lines 46-59, emphasis added).

Clearly, the very *last* modification of Sims' teaching that Sims would commend to one of ordinary skill is the abandonment of Sims' ibuprofen component; and even if the artisan ignored the express Sims teaching of **not** reformulating Sims according to symptoms, the artisan would only arrive at a vague and ill-defined composition that consisted of an antitussive and *optionally* an expectorant Such a composition is a far cry from the specifically claimed combination of carbetapentane *tannate* and guaifenesin. Therefore, Sims does not render the instant claims obvious.

Rather than challenge any of the above arguments the Examiner seeks to shift the burden of proof on to the Applicants by faulting Applicants for failing to offer evidence of an unexpected result. However, it is the Examiner that bears the burden of first demonstrating that a *prima facie* case of obviousness has been established before she can demand an unexpected result from the applicant. The need for "an unexpected result becomes an issue only when the examiner has established a prima facie case of obviousness." Ex parte Duke, 1995 WL 1718860, *6 (Bd. Pat. App & Int.). *citing* In re Piasecki, 745 F.2d 1468, 1472 (Fed Cir. 1984). In re Keller, 642 F.2d 413, 425 (CCPA 1981).

A motivation found *within* the prior art to make the proposed modification is one element of the three-prong test for establishing a *prima facie* case of obviousness. MPEP § 706.02(j). Insofar as the Examiner has failed to show **where** Sims contains the motivation to abandon its ibuprofen element, and to further select from among the

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universe of antitussives and expectorants the two exact components claimed, as the only actives, and the claimed amounts thereof, the Examiner has failed to establish that *prima facie* case of obviousness that would warrant Applicants' demonstration of unexpected results.

In view of the foregoing arguments all of the Examiner's rejections based upon the Sims reference have been adequately traversed, yet those arguments remain unrebutted.

The specification's disclosure supports the newly presented claim element of twice-a-day administration, in the last paragraph of page 3.

Applicants therefore submit that the instant application is in condition for allowance and they request its to prompt passage to issue.

The Office is hereby authorized to charge any fees due for independent claims in excess of three [37 C.F.R. 1.16(b)] to Deposit Account No.: 03-0678. It is believed that no further fee would otherwise be due. However, if any fee is due it should also be charged to Deposit Account No.: 03-0678.

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Serial No: 09/935,322
Filed: August 22, 2001

CERTIFICATE OF MAILING

Deposit Date: August 20, 2003

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8/20/03

Raymond E. Stauffer, Esq. Date

#191759 v1 - response to advisory action

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